

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Donald BELLGRAU et al.

Application No.: 10/825,282

Confirmation No.: 7928

Filed: April 14, 2004

Art Unit: 1633

For: VIRAL VECTORS ENCODING APOPTOSIS-
INDUCING PROTEINS AND METHODS FOR
MAKING AND USING THE SAME

Examiner: S. Kaushal

DECLARATION OF DONALD BELLGRAU
PURSUANT TO 37 C.F.R. § 1.132

MS Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Madam:

I, Donald Bellgrau, declare as follows:

1. I am named as an inventor for U.S. Application No. 10/825,282 ("the '282 application"). The other co-inventors named are Richard Duke and Jerome Schaack.
2. My current title is Professor of Immunology and Medicine and Program Leader in Immunology/Immunotherapy at the University of Colorado Denver.
3. I have reviewed the Office Action dated September 26, 2008.
4. I participated in a telephonic interview with Examiner Sumesh Kaushal on March 19, 2009, along with Richard Duke and patent counsel (Rob Traver, Richard Stern, Gladys Monroy, and Terri Shieh-Newton) to discuss the rejections in the Office Action.

5. During the interview, we discussed studies performed in a canine model of naturally occurring cancer with the Fas ligand (FasL) therapy disclosed in the '282 application.

6. The '282 application teaches the use of adenovirus vector encoding Fas ligand (Ad-FasL) for treating cancer, including metastatic cancer, at paragraphs [0021] and [0137].

7. The '282 application teaches the construction of recombinant adenovirus encoding FasL in Example 10 (paragraph [0199] *et seq.*)

8. The adenoviral vector encoding FasL (Ad-FasL) disclosed in the '282 application was used in a canine model of cancer.

9. There were two groups of dogs in this study, a control group and an experimental group. Both groups of dogs presented with naturally occurring osteosarcoma, which is a malignant bone cancer. Osteosarcomas are cancerous tumors in the bone.

10. The dogs in the control group had osteosarcoma with no visible metastases and were treated with standard-of-care ("SOC").

11. The SOC for a dog with osteosarcoma and no visible metastases is to amputate the dog's leg with the osteosarcoma and then to treat the dog with chemotherapy.

12. In the control group, there were no detectable signs of metastases at the time of amputation.

13. The dogs in the control group were evaluated at day 84 for event-free survival (death due to metastatic disease or cancer recurrence).

14. There was 72% survival of the dogs receiving SOC. Since the limb containing the bone that contained the tumor was amputated and since there was no visible sign of metastatic disease at the time of amputation, the death in the control group (28%) must be due to metastatic disease that was present at the time of amputation.

15. The experimental group of dogs with osteosarcoma received intratumoral Ad-FasL treatment for 10 days before receiving the SOC (amputation then chemotherapy) as the dogs in the control group.

16. All (100%) of the dogs in the experimental group who received Ad-FasL survived. None of the dogs with osteosarcoma who received Ad-FasL treatment died from metastatic cancer. This is a statistically significant result.

17. Therefore, Ad-FasL therapy is effective for treating metastatic cancer.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

3/28/09

Date



Donald Bellgrau